Electrophysiological challenges of cell-based myocardial repair.

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Public Summary:
Stem and progenitor cells (SPCs) hold great promise for the treatment of various cardiovascular diseases. Various SPCs have been shown to differentiate into primitive cardiomyocytes, yet the extent and precise mechanisms of SPC-based therapies remain complex and are the subject of many active research and clinical trials. Transplanted SPCs are a rich source of paracrine, angiogenic, and anti-apoptotic factors that could provide multiple beneficial effects on diseased host myocardium. Additionally, SPC-derived cardiomyocytes (SPC-CMs) have been proposed to be a potential source of cardiomyocytes for myocardial repairs, yet most SPC-CMs displayed heterogeneous and immature electrophysiological (EP) phenotypes with uncontrollable automaticity. Here, we present known arrhythmogenic mechanisms to illustrate that implanting these electrically immature and inhomogeneous CMs into hearts without further adequate maturation might carry arrhythmogenic risks. We also provide developmental insights of how regional and temporal cues influence the differentiation and maturation of various subtypes of cardiomyocytes during embryonic cardiogenesis. By simple injecting or infusing SPCs into hearts as currently performed in clinical trials, it is unrealistic to expect ischemic, diseased or failing myocardium to provide the complete set of developmental cues that occur in the early embryo, and even less so in the correct sequence. We hope that these EP and developmental knowledge will stimulate more basic research and carefully designed clinical trials to provide mechanistic insights of inducing maturation of primitive SPC-CMs after cell transplant. With proper maturation of transplanted primitive SPC-CMs, we should be able to develop a feasible and safe cell-based therapy for heart diseases.

Scientific Abstract: